PATHOBIOLOGY

PATHOLOGY SUMMARY

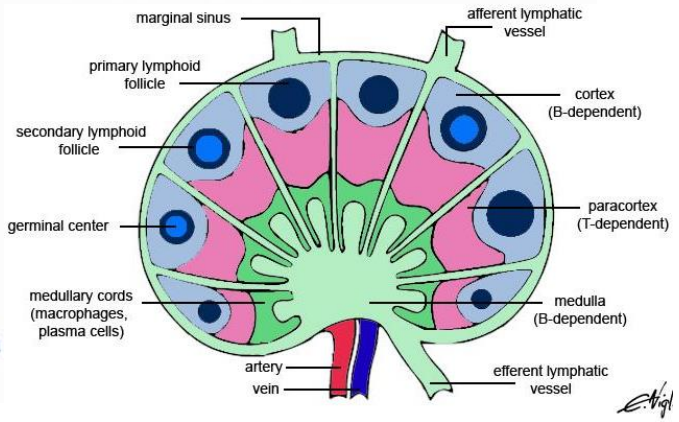
SideKick

YOUR BEST FRIEND

Diseases of the lymphoid system

Lymphadenopathy

- Lymphadenopathy
  - Neoplastic = malignant
    - 1.Malignant lymphoma
      - a. Hls
      - b. NHLs (+leukemia)
    - 2.Histiocytic neoplasm
    - Metastatic deposit "more common"
  - Non-neoplastic = Reactive
    - Acute
      - Types
        - Localized
          - Pharyngitis
          - Tonsilitis
          - Tooth infection
          - Enlargement of cervical lymph node
        - Generalized
          - Measles
          - Infectious mononucleosis
      - Clinically
        - 1.enlarged, tender
        - 2.redness of the overlying skin
      - Fate
        - 1.Complete resolution
        - 2.Fibrosis &scaring
        - 3.Abscess ... rupture_ sinus
    - Chronic
      - Specific
        1. Sarcoidosis
        2. Syphilis
        3. T.B
        4. Toxoplasmosis
        5. Crohn's disease
        6. Cat scratch
      - Non-specific:
        1. Follicular hyperplasia
        2. Paracortical hyperplasia
        3. Sinus histiocytosis



Chronic non-specific lymphadenitis:

	Follicular hyperplasia	Paracortical hyperplasia	Sinus histioyctosis
Causes	2- chronic infection & inflammation 3- Autoimmune disease 4- Early AIDS &HIV.	1- Viral 2- drugs	**1- Immune response to drainage cancer &its products**
Effect	Activation of B-cell → large germinal center containing: (lymphocyte-blast-, debris & histiocytes) + collar of small B-lymphocytes.	T-cells → proliferation & transformation to → Immunoblasts → encroach upon germinal center.	**1- Hypertrophy of endothelial cells → distention of the sinusoids.** **2- Infiltration with histiocytes**
Clinically	**Painless "not tender" lymph node.** **Frequent combination between 3 types is common .** **Common sites : axilry & inguinal**		

Malignant lymphomas:

They are primary malignant tumor of cells native to lymphoid tissue.

	Hodgkin's lymphoma	Non Hodgkin's lymphoma
Incidence	It occurs at any age with peak incidence (adolescence, middle & older age)	
Classification:	Histologically (microscopically) **1-Rye :** - LP (lymphocyte predominance) - MC (mixed cellularity) - LD(lymphocyte depletion) - NS (nodular sclerosis) **2-WHO** Rye + LR (lymphocyte rich)	**1-Working formulation of clinical usage.** **2-REAL (4 immunotype)** - **Neoplasm of immature B Cell (precursor)** - **Neoplasm of mature B Cell (peripheral)** - **Neoplasm of immature T Cell (precursor)** - **Neoplasm of mature T Cell and NK cell (peripheral)** **3-WHO** **REAL + HL**

Typical presentation	- Painless enlargement of the lymph node, localized to single axial group (cervical , mediastinal, paraaortic)	- **Painless (not tender) lymphadenopathy, localized or diffuse.** - **One third (35%) are extra nodal (bone marrow, oropharynx, GIT, skin)**
Mesenteric & Waldeyer's ring	Rare	**More common**
Systemic manifestation	It is of obscure causes. (fatigue, fever , night sweating , weight loss, pruritis).	———
Complication	1- Enlargement of the lymph node → Mediastinal compression 2- Bone marrow involvement = anemia 3- Decrease T,B lymphocytes → ↑↑suscpetability to infection & modification of tubercline test.	**1- compression on surrounding tissue** **2- pancytopenia = (↓↓ WBCs, RBCs, platelets)** **3- Immunological disturbance (autoimmune hemolysis, infection by opportunistics)** **4- spleen infiltration (hypersplenism)**
Spread	* Contiguity = station to station = serotyping pattern . * Single lymph npde → adjacent LNs → spleen → other organs (liver, bone marrow, GIT) . * The metastases take the form of irregular nodules leading to enlargement of liver and spleen.	*** Contiguity** **Single lymph node → (others, spleen, liver , bone marrow)** *** In bone marrow → spill over → leukemia like picture .**
Prognosis	Depends on : 1- clinical stage (the most important) 2- Histological type 3- age (younger is better) 4- systemic complication (better prognosis if absent)	

Notes about Hodgkin's lymphoma:

1- The characteristic cells:

Reed-Sternberg cells:

a- Shape:

*i- **Classical:***

Large (15-45 –m)

Cytoplasm: slightly eosinophilic

Nucleus: It is binucleated, 2 nuclei having overlapping halves, mirror images to each other .

Each nucleus has deep eosinophilic nucleolus surrounded by clear halo **(OWL–EYE)**

*ii- **Non-classical:***

1. **Mononucleated (lacunar cells)**
2. **Multi nucleus (pop corn cells).**

b- **It is diagnostic not pathognomonic:**

They are similar to those present in many conditions (Mycosis fungoides, Infectious mononucleases, NHLs)

So, there is another requisite for diagnosis which is according to: Non- neoplastic inflammatory background of cells (lymphocytes. Plasma cells and eosinophils).

2- Types:

	LP	MC	LD	NS
Age &Sex	Under the age of 35 Male	Male	Older age Male	Adolescence, young adult Female Site : lower cervical, supraclavicular, mediastinal
Prognosis	Excellent -	Intermediate	Poor	Excellent
Gross				nodes are *replaced by pale tumour *discrete. In some cases there is fibrosis surrounding the node &focal necrosis.
Microscopic	**Loss of the normal architecture.**			
	1- Infiltration of mature lymphocytes & histiocytes. 2- (RS) cells in few number.	1- Large number of RS cells + fewer lymphocytes than LP. 2- Large number of eosinophils, plasma cells , histioccytes.	1- Few number of lymphocytes + abundant RS cells or their pleomorphic variants.	1- Neoplastic tissue rich in (lacunar cell) 2- Collagen bundles , dividing lymphoid tissue into nodule.

3- Nature of the disease:

The nature and etiology is unknown; the target cell of neoplastic transformation has not been identified certainly.

As there are both:

1- Some features of neoplasms.

2- Inflammatory components.

The two accepted theories are:

1

- It is a malignant neoplasm.
- RS cells is the essential neoplastic element, coming from activated B&T lymphocytes.
- RS cells → cytokines → immunological inflammatory changes.

2

Infective cause → HL.

- EBV is suspected to have a relationship.

STAGING of HL & NHLs (Ann Arbor classification)		
Stage I	Single LN (I)	OR Single ELO (I_E)
Stage II	>	OR Limited ELOs (II_E)
Stage III	one of LN on both sides of the diaphragm (II) , may include spleen (II_s)	OR Limited ELOs (II_E) , (III_{Es})
Stage IV	With or without LN	Bone with widespread of ELOs .
N.B: 1-LN = lymph node, ELO = extra lymphatic organ. 2- All stages are further divides into A & B according to the systemic symptoms. 3- It is much more useful in HL than NHL.		

Burkitt's lymphoma

- It is endemic in Africa, but may occurs sporadically.
- It is related to EBV, present in children and young adult.
- It is extra-nodal in presentation.
- In African type → maxilla or mandible, Non-African type → abdominal tumor.
- Responds well with aggressive chemotherapy with long remission.

MYCOSIS FUNGOIDES & SEZARY SYNDROME

- It is a cutaneous T-cell NHL .
- Involvement of the skin is the hallmark

Diseases of the nervous system

Increased Intracranial Pressure (ICP)

Definition: increase mean CSF >200 mm water/ 15 mmHg when measured in the lateral decubitus position

Causes:

a) **Space occupying lesion:** (mass شئ واخد حيز او زي)

Intracerebral "جوا نسيج المخ نفسه"	Extracerebral "في الdura"
1- Hematoma, hemorrhage	1- hematoma, hemorrhage
2- Tumors	2- tumors
3- Infection forming an abscess	

b) **Obstructive Hydrocephalus**

تجمع لل ' CSF " جوا الجمجمة نتيجه لسبب انسدادي و هنشرحه بالتفصيل الدرس اللي جي

c) **Cerebral edema:** (fluid accumulation in brain)

1- Intracellular (Cytotoxic): reversible cell injury e.g. ischemia

2- Extracellular (vasogenic/related to blood vessels): increased capillary permeability due to inflammation, infection, trauma

Effects:

a) **Brain Herniation:**

	Trans-tentorial/ Uncinate	Subfalcine/ Cingulate	Tonsillar
part	Uncinate gyrus of temporal lobe	Cingulate gyrus of enlarged hemisphere	Cerebellar tonsils
site	Through opening of tentorium cerebelli	Under falx cerebri	Through foramen magnum
effects	1-compress 3rd cranial nerve (oculomotor) → relaxation of muscles → pupil dilatation and ptosis *on same side (ipsilateral)* 2-Compress pyramidal tract → motor paralysis of muscles *Opposite side (contralateral)* 3-Compress posterior cerebral artery → ischemia of area supplied by it → visual cortex	3-Compress anterior cerebral artery & its branches	2-compress respiratory centers in medulla oblongata 3-brain stem hemorrhage "Duret's hemorrhage"

b) Changes in skull bone:

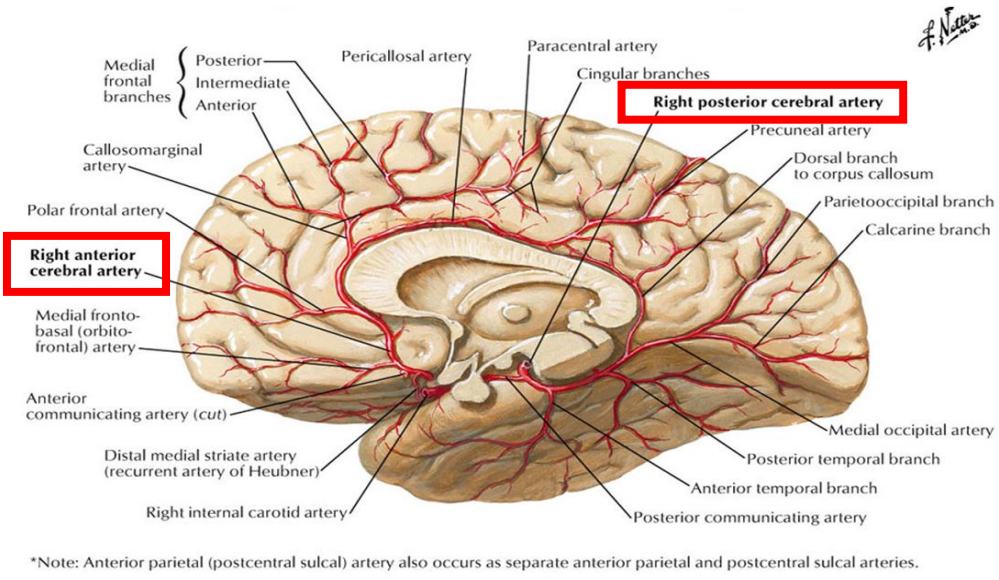
-adult → bone erosion on x-ray

-infant → head enlargement and delayed closure of fontanelles

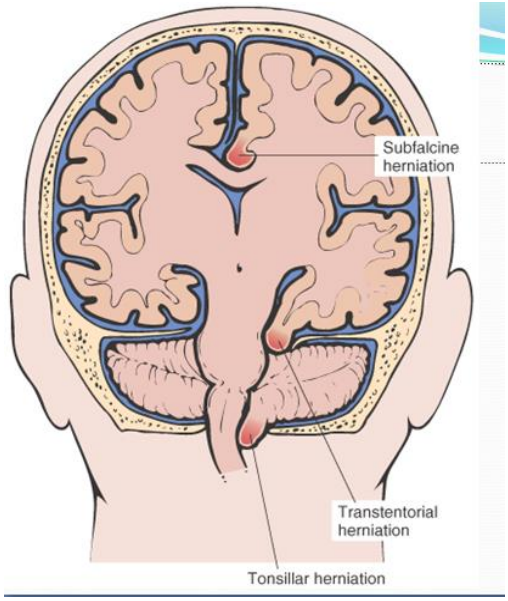
c) Vasomotor paralysis (permanent vasodilation of cerebral BVs)

Clinical Picture: مجموعة هتتحفظ وتتكتب في اي مكان نذكر فيه ارتفاع الضغط

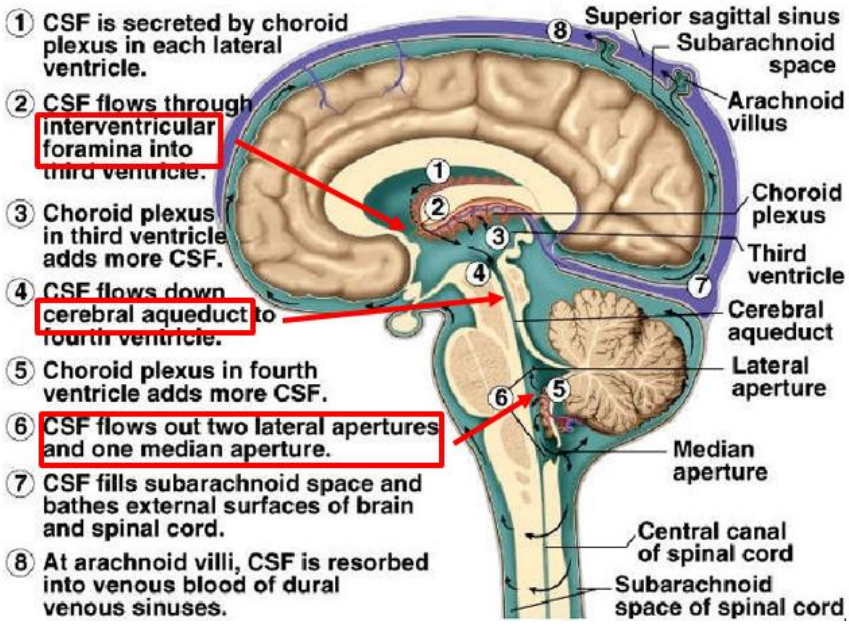
Headache, projectile vomiting, papilledema, blood pressure changes, coma



*Note: Anterior parietal (postcentral sulcal) artery also occurs as separate anterior parietal and postcentral sulcal arteries.



Normal CSF flow:



Interventricular foramina = foramen of Monro

Cerebral aqueduct = aqueduct of Sylvius

Lateral and median apertures = foramina of Luschka and Magendi

Hydrocephalus

Definition: accumulation of excessive *amount* of CSF in ventricular system

	With Normal CSF Pressure (compensatory/exvacuo)	With increased CSF pressure	
		Non-communicating	communicating
Pathology	CSF volume increases following decrease in brain tissue volume (atrophy) to fill the empty space (exvacuo), thus total pressure intracranially remains unchanged	Obstruction prevents passage of CSF from area of production to subarachnoid space where it's absorbed	1)increased CSF secretion 2)decreased CSF reabsorption in subarachnoid space *"Without any obstruction in the ventricular system"*
causes	1-localized atrophy: Infarct→ area supplied by blocked artery undergoes necrosis 2-diffuse atrophy: Alzheimer's → general atrophy of neural tissue, widening ventricles, widened sulci	1) Occlusion of foramena of Luschka and Magendie: Due to cerebellar tonsil descend into spinal canal "Arnold Chiari malformation" 2) Occlusion of aqueduct of Sylvius: *-congenital:* a) stenosis *(partial narrowing)* b) atresia *(complete occlusion)* *-acquired:* a) neoplasm/cyst pressure b) gliosis & inflammation	1)increased secretion: -choroid plexus papilloma 2)decreased reabsorption: - healing of meningitis by fibrotic adhesions in subarachnoid space - dural sinus thrombosis leading to deficient absorption due to blood stagnation
Effect		- adult: increased ICP - child: enlarged head, delayed closure of fontanelles (thus delaying increase in ICP) + progressive brain atrophy	

Cerebrovascular Diseases

Cerebrovascular Diseases

1- **Ischemic encephalopathy:** generalized brain hypoxia/ischemia

   Boundary Zone Infarct: area already with poor blood supply, when generalized ischemia occurs, it will be the 1st affected → infarct

2- **Infarction:** occlusion of certain BV→ only supplied area is affected "the most common"

3- **Spontaneous** *"non-traumatic"* **Intracranial Hemorrhage:**
   * intracerebral/hypertensive *(inside brain tissue)*
   * subarachnoid/aneurysmal
   * mixed

Traumatic Intracranial Hemorrhage:
* Parenchymal *(inside brain tissue)*
* Epidural hematoma
* subdural hematoma

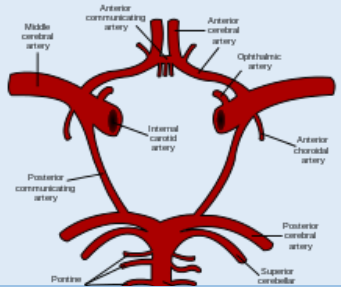
	Ischemic Encephalopathy	Infarcts
cause	*Generalized hypoxia due to:* 1-venitlation disorder: problem in lung *"e.g. fibrosis"* leading to low oxygen content carried by blood 2-decreased cerebral perfusion: not enough blood reaching the brain due to: * decreased systemic blood pressure (low blood volume) * cardiac arrest (heart unable to pump) * increased intracranial pressure (causes pressure on BVs obstructing them) 3-cerebrovascular disease: problem with vessel itself e.g. atherosclerosis, endarteritis	*Block of 1 vessel due to:* 1-Atherosclerosis & Thrombosis of: Large BVs [Internal carotid, Middle cerebral, Basillar] 2-Emboli: * Infective Endocarditis vegetations * Arterial thrombi * ventricular thrombi 3-Others: * Vasculitis * Compression of artery due to herniation * border zone infarcts

Clinical features	Mild: transient confusion after ischemia, followed by full recovery Severe: coma, + generalized loss of cortical functions	a) thrombosis: *gradual* transient ischemic attacks with clouding consciousness and coma b) emboli: *rapid/acute* + focal manifestations of involved area e.g. hemiplegia and dysarthria

Morphology of brain infarct:

	> 6-12 hrs.	48-72 hrs.	Weeks/months
gross	Anemic/pale, softened infarct "change in color"	- line of demarcation - edema around the lesion may lead to herniation,,,	- resolution: liquefaction and cyst formation surrounded by glial reaction → honey-comb - meninges thick & opaque
micro	- ischemic cell injury + necrosis - neutrophil infiltration	- prominent BV VD - neutrophils replaced by macrophages	- gliosis replaces necrotic tissue and encloses cyst

Spontaneous non traumatic intracranial hemorrhage:

	intracerebral/parenchymal:	Subarachnoid/aneurysmal: *(Not within brain parenchyma, BV on external surface of brain below arachnoid)*
Causes:	1) hypertension (60+ years) 50% Site: *lenticulostriate arteries (inside brain parenchyma) around basal ganglia and internal capsule*	1) rupture of congenital Berry aneurysm زي "التوت" Site: *arterial bifurcations mainly in circle of Willis;* *- Anterior communicating artery* *- Junction of post communicating & internal carotid* *- Bifurcation of middle cerebral artery* 

	2) other causes: - arteriovenous malformation - rupture of Mycotic aneurysms - bleeding & coagulation disorders - bleeding into tumors	* ***RULE*** → aneurysms always form at bifurcations 2) other causes: - arteriovenous malformation - Mycotic aneurysm - Atherosclerosis
Patho-genesis:	1) Hypertension weakens wall of artery forming microaneurysms which then rupture *"charcot-bouchard microaneurysms"* **Site**: *bifurcation "**RULE**" of small intraparenchymal arteries* 2) Changes occurring in hypertension e.g. benign arteriolosclerosis or hyalinosis, which weaken wall further, leading to rupture of affected arteries.	Berry aneurysms: @ birth: defect of media of artery due to discontinuity of smooth muscles Aneurysm forms with progressing age **Chances of rupture:** - with increasing age - greater than 10 mm - acute increase in ICP (stool strain, exercise, sexual intercourse)
Morph-ology:	***External***: brain is asymmetrical, one hemisphere enlarged due to hematoma or associated edema Enlargement may cause flattening of gyri, trans-tentorial herniation, or midbrain displacement to the other side. ***Cut surface:*** (affect ventricular system) blood clot that may: A) rupture into ventricular system → blood in CSF → meningeal irritation B) mass distorting ventricles on same side (ipsilateral) C) mass occluding foramen of Monro or aqueduct of Sylvius → acute obstructive hydrocephalus with increased ICP	
Fate:	40% mortality Resolution: macrophages digest clot leaving cavity surrounded by gliosis	25-50% die re-bleeding is common in survivors Resolution: blood resorbed and replaced by fibrosis, may lead to hydrocephalus

Prog-nosis:	good, hemorrhage compresses tissues but doesn't destroy them	re-bleeding is common in survivors
Clinical-ly:	1) increase ICP 2) papilledema 3) local neurological deficiency depending on area affected e.g. hemiplegia from pyramidal tract affection	1) increases ICP 2) meningeal irritation e.g. neck rigidity (meningeal irritation تجميعة)

Traumatic intracranial haemorrhage:

	Epidural hematoma	Subdural hematoma	
Site:	between dura and bone "internal surface of skull"	between dura and outer layer of arachnoid	
Cause:	Fracture "pterion" → rupture of middle meningeal artery	torn superficial bridging veins between convexities and dural venous sinuses	
Nature:	arterial blood	venous blood	
Fate:	- expand rapidly (arterial blood under pressure) - increased ICP and herniation	- slow expansion (vein) - mild increase in ICP	
Clinical:	lucid interval where no symptoms show الديورا بتكون قوية كفاية و لسه قادرة تشيل كمية الدم ومتسيبوش يضغط على المخ ف مش بيبان اي اعراض Increased ICP symptoms	slow onset and mild increased ICP "space occupying lesion --> brain atrophy"	
Types		acute: -clotted blood -clear history of trauma	chronic: -liquid blood -minor neglected bilateral trauma, -elderly or alcoholics (brain atrophy strains on veins)

Healing: hematoma is surrounded by granulation tissue (fibroblasts and collagen)
- Fibroblasts → mature collagen
- BVs → poorly developed → may rupture and expand hematoma

Parenchymal injury:

- **Concussion (ارتجاج):** transient loss of consciousness following head trauma, usually with complete recovery.
- **Contusions (كدمات):** bruises or crests of gyri either at the site of impact (coup) or at a point opposite (countrecoup), characterized by foci of hemorrhage.
- **Laceration:** tearing of the brain tissue at the site of trauma or at opposite site.
- **Coutrecoup:** results from impaction of the brain against the rigid dural septa & skull bone, as well as sliding of cerebral hemispheres with each other.

Effects of trauma:

Acute:
- brain edema
- herniation
- infection

chronic:
- epilepsy
- personality changes
- meningeal fibrosis & hydrocephalus

Infections of CNS

A) **Leptomeningitis** (pia + subarachnoid space + arachnoid)

B) **Encephalitis** (brain parenchyma)

C) **Epidural or subdural infections** (spreading from adjacent structures only)

Routes of infection:

1. Blood
2. Ascending with peripheral nerves
3. Direct penetrating trauma
4. Direct spread from adjacent structures through bone eg sinuses, mastoid, middle ear
5. Iatrogenic lumbar puncture

A)Leptomeningitis:

	acute purulent meningitis	acute lymphocytic meningitis	chronic meningitis
Agents:	**Bacteria;** - Neonates: → **E. coli** *(flora of mother during birth)* - Children: → **H. influenza** - Adolescents: → **N. meningitides** - Epidemics in all ages: → **pneumococci & Gm -ve bacilli** - Surgical shunts to treat hydrocephalus: → **staphylococci**	**Viruses;** e.g. mumps, EBV	**Bacteria**: e.g. TB, T. pallidum, brucella **Fungi**: candida
Gross:	- Meninges: congested, dull opaque - Subarachnoid space: creamy exudate *(turbid due to suppuration)*		- Meninges: opaque, thickened (fibrotic) - Subarachnoid space: gelatinous or fibrous exudate, dense fibrous adhesions
Micro:	- congested - Infiltrated by neutrophils, lymphocytes, fibrin		a) nonspecific: exudate with cells *(lymphocytes, fibroblasts, plasma cells, histiocytes)* b) specific: Tb: *granuloma + caseation* Syphilis: *endarteritis obliterans*
Clinical:	1-infection general signs: fever, hemorrhagic rashes 2-*meningeal irritation:* *headache, photophobia, irritability, neck stiffness* تجميعة تتقال في اي حته فيها اريتيشن	less severe, self limited	
CSF Picture			
Pressure	High	High	High
Gross	Turbid	Clear	Clear or caseation
Cells	Neutrophils	Lymphocytes	Both + epitheliod cells
Protein	High *(cellular breakdown & pus)*	Slightly high	V.high (caseation)
Glucose	v. low (consumed)	Normal	Low
Chloride	Normal or low	Normal	v. low (consumed by TB)

Complications of meningitis (acute purulent):

a. **spread:**

- Inside CSF passages:

1- ependymal surface of ventricles→ ventriculitis

2- subdural/epidural

- To vessels:

3- leptomeningeal veins and sinuses → thrombophlebitis (inflammation of vessel & thrombus formation)→ vascular occlusion→ brain infarct of hemorrhagic type (i.e due to vein block)

4- blood spread, leading to:

- septicemia w/intracranial hemorrhage and bilateral adrenal hemorrhage, due to meningococcal meningitis "*waterhouse friderichsen syndrome"*
- localization in different tissues: arthritis, endocarditis, pericarditis

b. **Healing:**

1- Arachnoid fibrosis → hydrocephalus

2- compress cranial nerves due to fibrosis → palsy/weakness e.g. squint

3- obliterative endarteritis in syphilis → infarct

B) encephalitis:

Bacterial brain abscess: Localized suppurative inflammation of brain parenchyma

Causative organisms: staph, strept, anaerobic

Mode of infection:

1-haematogenous: bact endocarditis, lung abscess, bronchiectasis
2-direct implantation by trauma
3-direct extension from adjacent structures

Sites:

middle ear infection--> temporal lobe and cerebral hemispheres
Paranasal sinusitis --> frontal lobe

Morphology:

solitary (direct) or multiple (by blood) cavities filled with puss
Surrounded by gliosis and fibrosis

Clinically:

- increased ICP
- focal manifestations

Complications:

rupture of abscess → ventriculitis, thrombophlebitis, meningitis

**look at page 168

Nervous System Tumors

	1. Primary	2. Metastatic
%	50-75%	25-50%
Site	70% in cerebral hemispheres	1ry site: Lung, breast – skin melanoma- GIT, Kidney
other	- Cause death if located in critical region or compress medulla - rarely metastasize outside CNS but may spread through subarachnoid space	- single / multiple - may be the 1st manifestation of cancer

Primary tumors:

Neuroepithelial	Embryonal	Cranial Nerves	Meninges	Sellar Region
•Gliomas •Neuronal Tumors •Choroid Plexus tumors •Tumors of pineal region	•Medulloblastoma	•Schwannoma •Neurofibroma •Malignant Periphral Nerve SHeath Tumor MPNST	•Meningioma	•Pituitary Adenoma •Cranio-pharyngeoma

Clinically:

1-increased ICP
2-Focal deficit at site of tumor
3-seiures

Primary Tumors → Neuroepithelial → Gliomas → **Astrocytomas:**

- most common 1ry brain tumor
- Diffusely infiltrating astrocytomas progress from low to higher grades with increasing anaplasia
- may infiltrate large regions→impossible curable resection

	Diffusely Infiltrating Astrocytoma			Localized astrocytoma
	80% of 1ry tumors Adults 40-60 Site: cerebral hemispheres,*& cerebellum, brainstem, spinal cord*			Benign Children cerebellum, optic nerve
	Diffuse astrocytoma GII	Anaplastic Astrocytoma GIII	Multiform Glioblastoma GIV	Pilocytic Astrocytoma (tumor of 2s) GI
gross	Poorly defined Grey infiltrative Few cm→large Firm→soft/gelatinous		Well demarcated Variegated appearance 1- firm white 2- soft yellow necrotic 3- Cyts & hemorrhage	Well circumscribed 1- cystic 2- mural solid nodule in wall of cyst
micro	- Mild increase cellularity - mild nuclear atypia - NO mitosis - NO vascular proliferation or necrosis	- moderate - moderate - mitosis present - NO vascular proliferation or necrosis	-marked - marked pleomorphism - mitosis present - vascular proliferation and necrosis present	- Biphasic: 1-loose microcystic 2-fibrillary areas of bipolar cells with hair-like processes - Eosinophilic structures 1-Rosenthal fibers 2-granular bodies

Primary Tumors → meninges → **meningioma:**

Incidence: adult, females > males
origin: meningothelial cells of arachnoid
site: -intracranial: external surface of brain, skull base, ventricular system
-intraspinal
Risk factors: previous radiation therapy
Behavior: Slowly growing
contain progesterone hormone receptors → grow rapidly during pregnancy
Gross:
- rubbery or firm: a)discrete lobulated mass attached to dura
b)sheet-like meningioma en plaque
- bone shows thickening/hyperostosis

Micro of benign meningioma GI: multiple patterns with no prognostic significance
1-meningothelial: syncytial clusters of cells, no visible borders
2-Fibroblastic: elongate cells, collagen deposition
3-transitional: both 1 and 2
4-psammomatous: + psamomma bodies

Primary Tumors → Cranial Nerves/Peripheral Nerve Sheath Tumors

Benign	Malignant
1- **Schwannoma:** local compression of involved nerve and surrounding structures **2- Neurofibroma:** mixture of Schwann cells, fibroblasts, perineural cells	**Malignant Peripheral Nerve Sheath Tumor MPNST**

Diseases of Bone

Diseases of Bone:

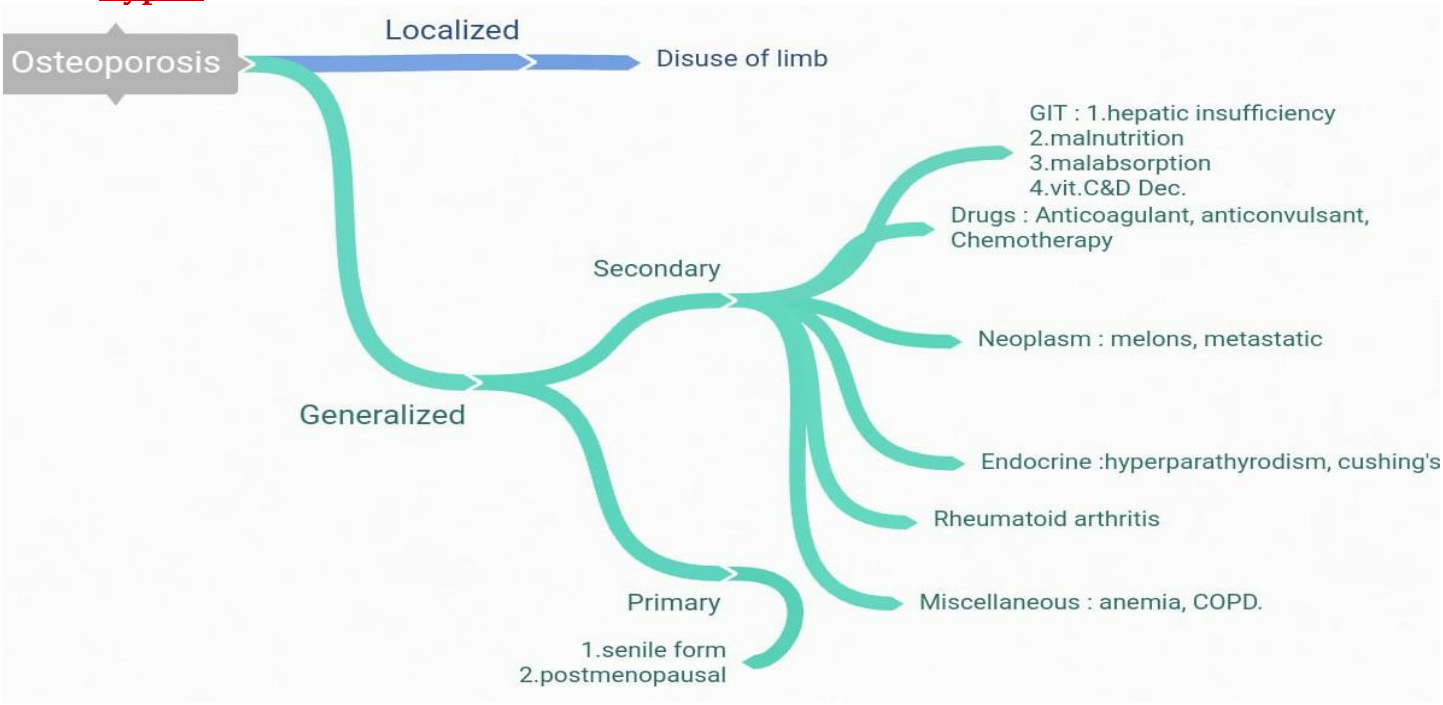
A) **Osteoporosis**

B) **Osteomyelitis**

C) **Bone Tumors**

A) Osteoporosis:

Types:



Morphology:

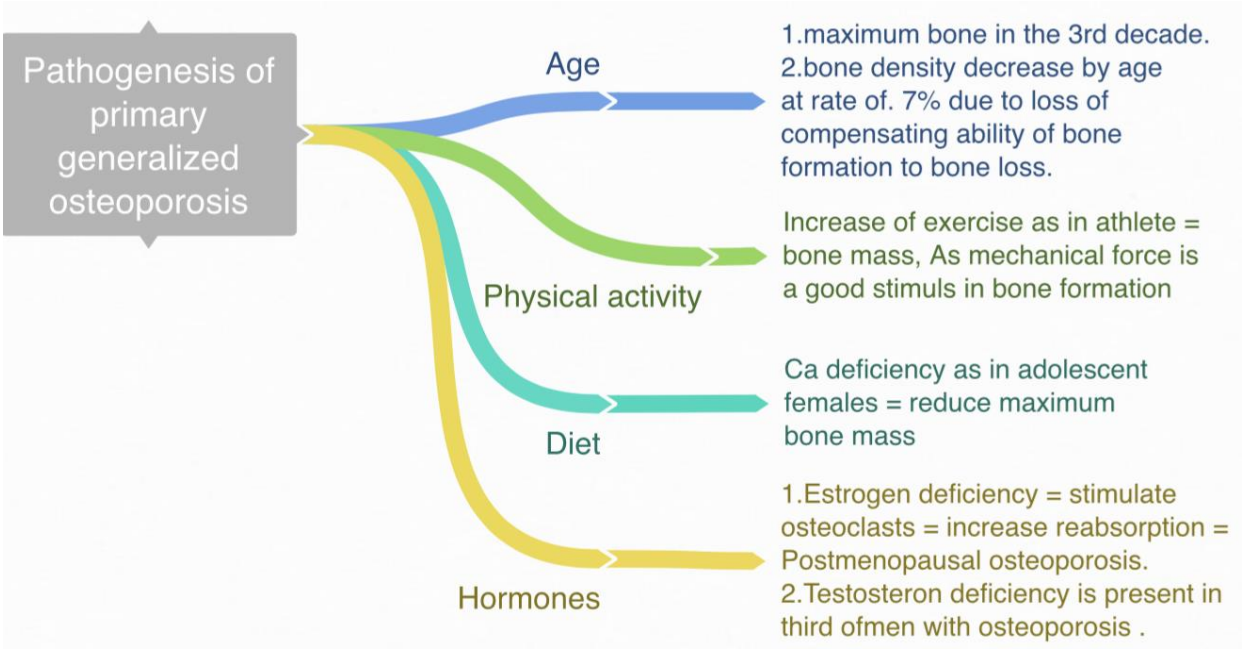
1- The cortex is thinned.

2- Haversian systems widened.

3- Normal composition of bone protein and minerals.

Pathogenesis:

Decrease in formation + increase in loss => Decrease in total bone matrix.



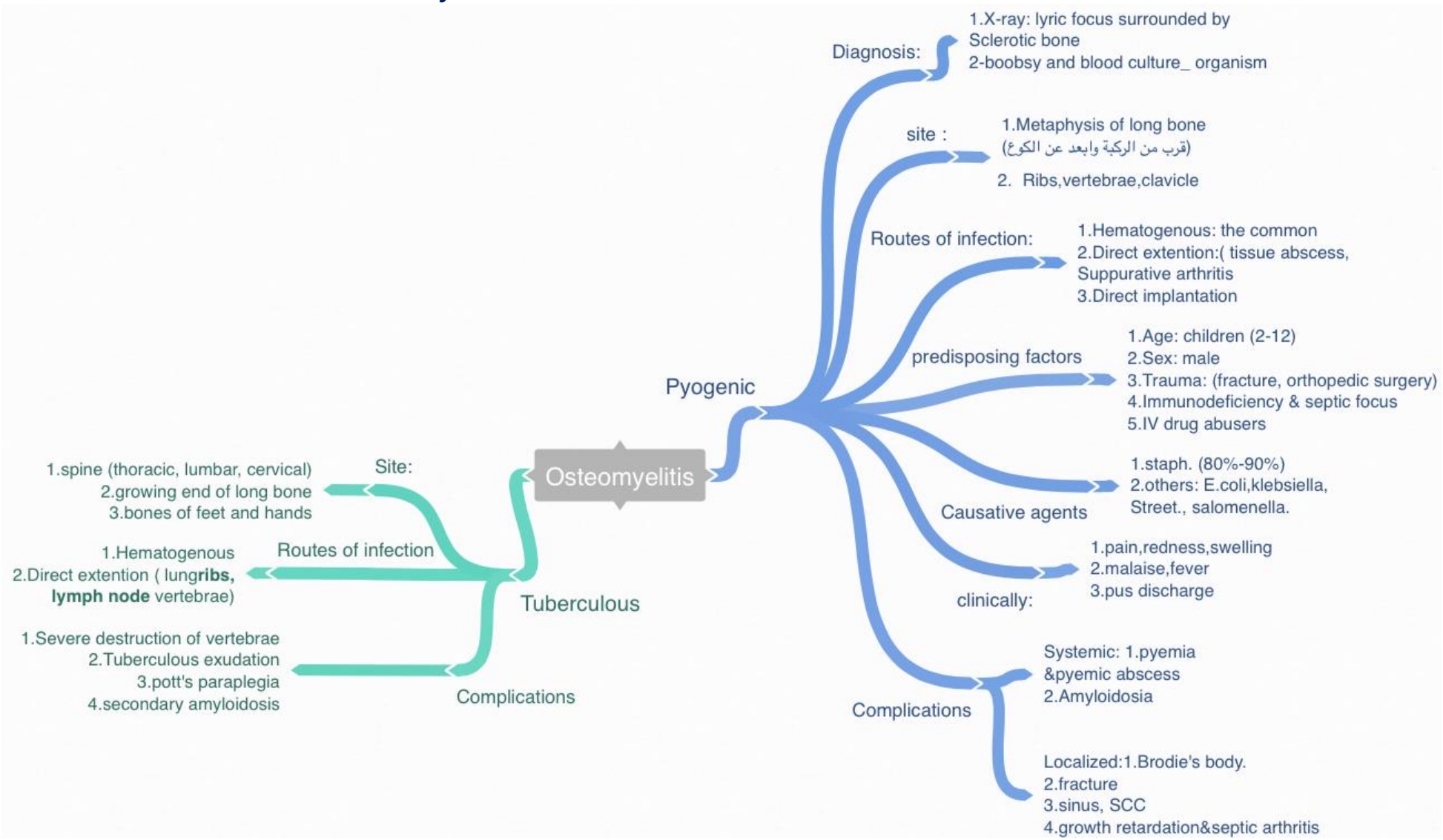
Clinically:

1- Asymptomatic.
2- Pain, loss of height.
3- Fractures of weight bearing bones (vertebrae, wrist, femoral neck)
4- Lordosis ,kyphoscoliosis.

Diagnosis: (difficult):

1- X-ray (only after loss of 30-40%)
2- Blood level of Ca &alkaline phosphatase is normal.
3- No symptoms until advanced cases.

B) Infection of bone (osteomyelitis):



Pathogenesis of pyogenic osteomyelitis:

1. **In bone marrow:**
   Suppurative reaction → ↑↑↑ intraosseous pressure => spread of infection:
   - longitudinally → bone shaft
   - horizontally → endosteum → haversian system → periosteum
2. **Exudation & edema → compress BVs → vascular thrombosis & ischemia → necrosis of a segment "Sequestrum"**
   **** Sequestrum may by:**
   - reabsorbed (if small)
   - sloughed → form foreign body → dissect through a sinus
   - In chronic osteomyelitis surrounded by a rim of thick reactive bone **"Involucrum"** → ***Brodie's abscess***

3. **In children: the periosteum is loosely attached to:**
   - Cortex → periosteal abscess → sinus formation
   - Articular margin → sub-periosteal & trans-epiphyseal spread of infection → suppurative arthritis

Pathogenesis of tuberculous osteomyelitis:

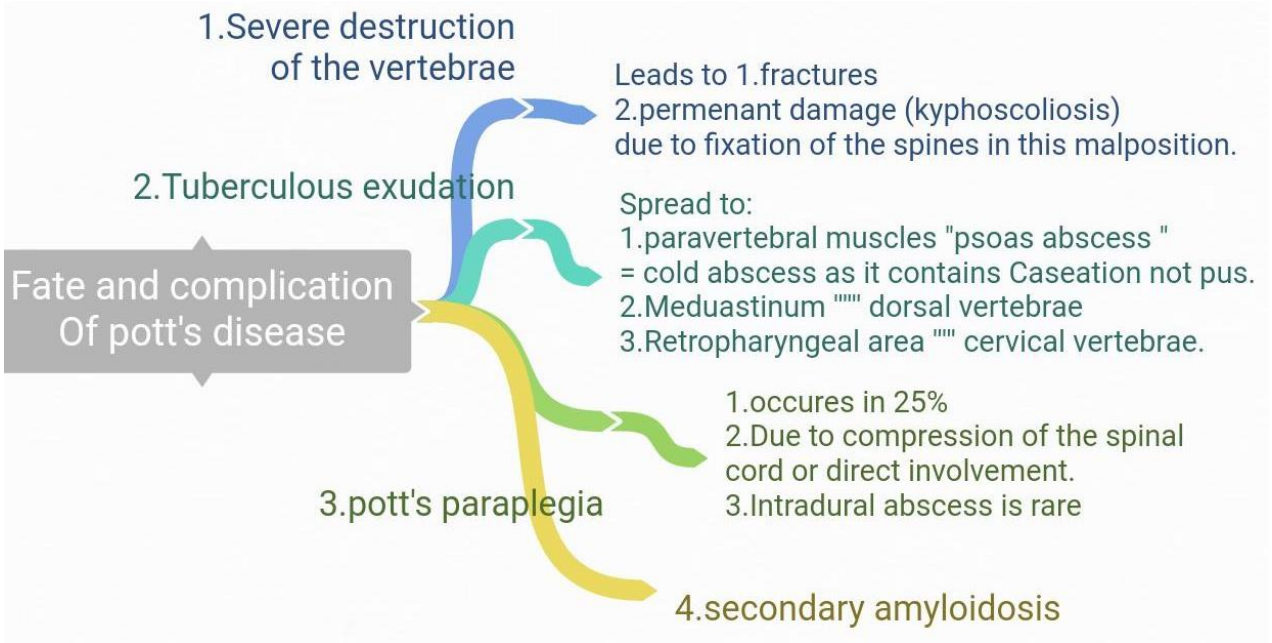
from bone marrow cavity → inflammation & necrosis of cortex → multiple sinuses *"soft tissue → skin"*

Tuberculosis (pott`s disease) of spine = Tuberculous spondylitis.

Age : children and young adult.
Sex: male > female
Thoracic > lumbar > cervical .

Morphology:
Gross:
1- multiple organ affection due to invasion of epiphyseal cartilage.
2- Necrosis & caseous granular debris.

Microscopically:
Destructive &repair+ caseous necrosis + tubercles.



Tuberculous Dactylitis

1- It involves small bones of feet and hands.

2- Destruction of the bone, as it is replaced by tuberculous granulomatous reaction → fusiform digits.

c) Bone Tumors:

	Osteoma	Osteoid osteoma	Osteo-blastoma	Osteo-sarcoma	Osteo-chondroma	Chondroma	Chondro-sarcoma	Giant cell tumor	Ewing`s tumor	Plasma cell (multiple) myeloma
Age	Adult	Children	Children	Primary: children Secondry: adult	children	Adult (30-50) At any age	Adult	Adult (20-40)	Children	50-60
Sex	Male > female					Male = female		Female > male	Male > female	Male = female
Site	Skull ,facial bone	Metaphysis of long bone (towards knee, far elbow) cortical	Vertebral column Medullary	Metaphysis of long bone (towards knee, far elbow)	Metaphysis of long bone (towards knee, far elbow)	Metaphysis of tubular bone of hands and feet Medullary > cortical	Central skeleton (ribs ,shoulder ,pelvis) Medullary > cortical	Epiphysis of long bone	Diaphysis of long bone Flat bone of pelvis Medullary	Vertebrate ,ribs, Skull ,pelvis ,clavicle ,scapula, femur. Medullary
Gross	Round ,bosselated ,sessile	Small ,oval mass *Necrosis & hemorrhage*	Larger	1-fusiform, "mutton leg" appearance" 2-necrosis & new bone formation. 3-hemorrage &cysts 4-invading soft tissue.	1-mushrome shape 2-lateral growth of bone (cortex &medulla) 3-cap of cartilage. 4-single or multiple.	1-well circumscribed 2-grey-blue mass 3-single(common), multiple	1-Large,lobulated 2- white-blue mass 3- hemorrhage &calcification 4- gelatinous	1-large 2-red-brown 3- necrosis &residual bone without new bone formation 4-cystic changes 5-single (common) , multiple.	1-protruding soft tissue mass 2-tan-white 3-hemorrhage & necrosis	1-focal lesion 2-Defect filled With soft, red, gelatinous tissue

Micro	Densly sclerotic bone (lamellar &woven)	1-trabeculae of woven bone &rim of osteoblast 2-nidus of osteoid+/- minerals 3- stroma: C.T + dilated capillaries.		1-malignant osteoblast(spindle/pleomorphic) 2- Giant cell 3- homogenous pink matrix	1-outer benign cartilage 2-inner bone trabeculae.	1- Hypocellular cartilage 2- chondrocytes are normal ,irregular dispersed in lacunar space	Malignant cells (well differentiated / poorly differentiated)	1-Cells: -mono-nuclear (neo-plastic) - Giant cell (reactive) 2- stroma: scanty + hemo-rrhage & necrosis	1-cells: small ,uniform, > lymphocyte ,clear cytoplasm, form pseudoresset. 2- stroma: scanty+ hemorrhage &necrosis	1-increase plasma Cell number =90% of marrow cells. 2-cells: well differentiated /pleomorphic
Clinically	1-Slowly growing 2- cosmetic ,air sinus ,brain ,eye ,oral cavity.	Pain at night relieved by aspirin.	Pain difficult to localized. Local recurrence **Osteo-sarcoma** is rare	1.Progressive enlarging ,painful mass. 2-metastasis to lung.	1-Slowly growing 2-pain: - Fracture - Pressure on nerve	1-silent (common) 2-pain ,deformity, fracture.	1-Progressive enlarging ,painful mass. 2- depend on differentiation	Un-predictable Recurrence , Sarco-matous behaviour	Enlarging , tender ,warm mass. Fever ,leukocytosis	1-pain & fracture 2-Anemia 3-Pneumonia 4-pyelo-nephritis
Radiograph		Nidus → radiolucent Rim of sclerotic bone		1-codman`s triangle 2- radiating bone spicule (sun ray appearance)				1-large, lytic, "soap like" 2- cortex is destroyed. 3-bulging soft radiolucent tumor	-lytic - reactive bone deposition "onion-skin appearance"	
Prognosis				According to: 1. Size 2. Histological type, fibroblast type with best prognosis	Multiple hereditary exosteosis 1% → **chondro-sarcoma**	1-solitary: innocent. 2-Multiple: 30% → **chondro-sarcoma**	According to: 1. Size 2. Differentiation		1-Aggressive 2-with treatment: 5 years survival rate is 75%	Variable

Important Notes:

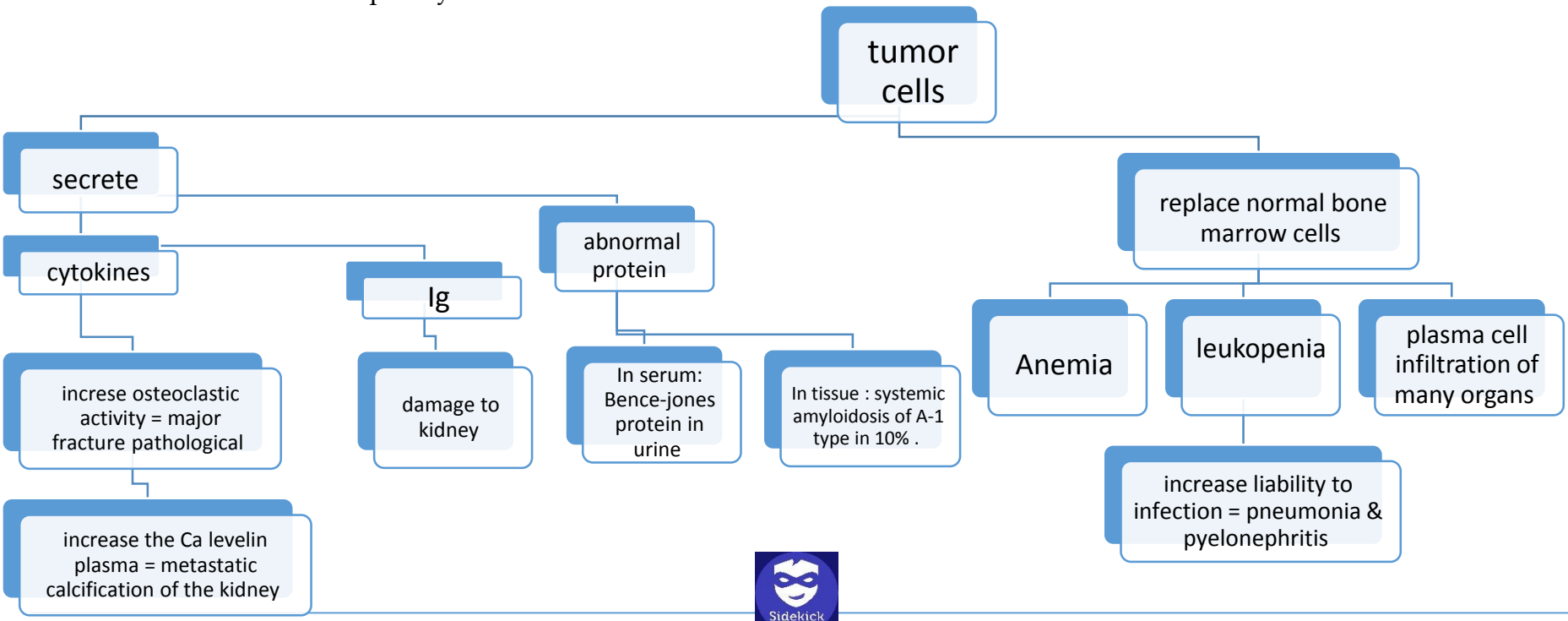
1- Both osteosarcoma and chondrosarcoma are dividing into primary and secondary, the latter in osteosarcoma is due to bone diseases (eg:paget`s),while in chondrosarcoma (25% of chondrosarcoma) is due to either multiple enchondromatosis or exosteosis.

2- The most common:
   - Malignant tumor in bone = metastatic.
   - Primary malignant tumor excluding multiple myeloma = osteosarcoma .
   - Second common in adult = chondrosarcoma.
   - Second common in children = Ewing`s disease.

3- Osteochondroma stops growing when normal growth stops.

4- Multiple osteochondroma always autosomal dominant hereditary disease , while multiple chondroma may be familial or not.

5- Nature & effect of multiple myeloma:



Metastatic tumors of bones: